REMARKS

The title of Example 31 on page 149 of the specification was corrected hereinabove. The explanation for this correction is as follows.

Compound 1-132 found in Table 1 and Example 31 was misnamed in the title of Example 31. The compound was named as 4-[1-dimethylamino-3-(4-**trifluorophenoxy**)propyl]phenyl dimethylcarbamate. It should have been named 4-[1-dimethylamino-3-(4-**fluorophenoxy**)propyl]phenyl dimethylcarbamate.

The correct name is clear from the nature of the starting material, namely, 4-[3-(4-**fluorophenoxy**)-1-methylaminopropyl]phenyl dimethylcarbamate, and the reaction carried out upon this starting material, which in fact converts the methyl amino to the dimethyl amino, as shown in Example 3. The compound is correctly named on page 56, lines 5 to 6 of the specification, where it is stated to be compound 1-132.

Page 201 of the specification was amended to correct a minor clerical error.

As set forth on page 3, lines 16 to 18 of the Office Action, the undersigned had a telephone interview with the Examiner on November 7, 2005 regarding the extent of the claimed subject matter that the Examiner was willing to search and possibly allow. The result of the aforesaid telephone interview is set forth on page 3, lines 7 to 12 of the Office Action.

The undersigned also had a telephone interview with the Examiner on January 3, 2006 regarding the initial erroneous sending of the Office Action to another firm.

The compound claims have been amended hereinabove to conform to the scope set forth on page 3, lines 7 to 12 of the Office Action.

Claim 83 was amended to correct a minor clerical error (see Example 48 on pages 156 to 157 of the specification; Example 98 on page 185 of the specification; Example 101 on page 187 of the specification; and Example 121 on page 199 of the specification).

New claim 120 is supported in the specification as set forth in the following table:

Compound	Table - compound Number	Synthetic example
4-[3-(4-fluorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-75	30
4-[3-(3-fluorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-76	68
4-[3-(4-chlorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-78	82
4-[3-(3-chlorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-79	38
4-[3-(4-nitrophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-92	48
4-[3-(3,4-difluorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-102	54
4-[3-(4-chloro-3-fluorophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-104	55
4-[3-(2-chloro-4-nitrophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-108	124
4-[1-dimethylamino-3-(4-fluorophenoxy)propyl]phenyl dimethylcarbamate	1-132	31
4-[1-dimethylamino-3-(3-fluorophenoxy)propyl]phenyl dimethylcarbamate	1-133	70
4-[3-(4-chlorophenoxy)-1-dimethylaminopropyl]phenyl dimethylcarbamate	1-135	41
4-[3-(3-chlorophenoxy)-1-dimethylaminopropyl]phenyl dimethylcarbamate	1-136	51
4-[1-dimethylamino-3-(4-nitrophenoxy)propyl]phenyl dimethylcarbamate	1-149	89
4-[3-(3,4-difluorophenoxy)-1-dimethylaminopropyl]phenyl dimethylcarbamate	1-159	152
4-[3-(2-chloro-4-nitrophenoxy)-1-dimethylaminopropyl]phenyl dimethylcarbamate	1-165	129
4-[3-(4-nitrophenylsulfanyl)-1-methylaminopropyl]phenyl dimethylcarbamate	1-43	153
4-(1-methylamino-3-p-toluyloxypropyl)phenyl dimethylcarbamate	1-82	40
4-[1-methylamino-3-[(4-trifluoromethyl)phenoxy]propyl]phenyl dimethylcarbamate	1-85	17
4-[3-(4-cyanophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate	1-91	56
4-[1-methylamino-3-(3-nitrophenoxy)propyl]phenyl dimethylcarbamate	1-94	53

New claim 121 recites compound 1-78 (see Table 1, page 25 of the specification and Example 16 (page 139 of the specification)).

New claim 122 recites the compound of Example 98 (see page 185 of the specification).

New claim 123 recites the compound of Example 82 (see page 176 of the specification).

New claim 124 recites the compound of Example 98 (see page 185 of the specification),

New claim 125 recites the compound of Example 82, (see page 176 of the specification).

New claim 126 recites the compound of Example 121 (see page 199 of the specification).

New claim 127 recites the compound of Example 164 (see page 218 of the specification).

Claim 110 was replaced with new claim 128

New claims 130 recites features of claims 128 and 129.

New claims 131 and 132 replace previous claim 118.

New claim 133 replaces features of claim 130.

It is noted that compound 1-92 in Table 1 and in Examples 48, 98, 101 and 121 (see claim 83) has the following two alternative names:

a) 4-[3-(4-nitrophenoxy)-1-methylaminopropyl]phenyl dimethylcarbamate (see, for example, the compound on page 55, lines 4 and 5 from the bottom of the specification).

b) 4-[1-methylamino-3-(4-nitrophenoxy)propyl]phenyl dimethylcarbamate (see Examples 48, 98, 101 and 121).

Applicants are pleased to note that the Office Action did not include any prior art rejections.

Claims 46 to 92 and 118 were objected to for containing non-elected subject matter (see the middle of page 5 of the Office Action). Withdrawal of such objection is respectfully requested in view of the above claim amendments.

Method claims 93 to 118 were rejected under 35 USC 112, first and second paragraphs, for the reasons set forth on pages 4 to 5 of the Office Action.

To reduce issues, claims 93 to 101 were canceled.

Regarding the last two sentences on pages 4 and 5 of the Office Action, the "test" compounds in table 6 on pages 270 to 271 of the specification correspond respectively to the example compounds in the specification.

Claims 102 to 109 and 128 to 130 are directed to a method of treatment of depression, Huntington's chorea, Pick's disease, tardive dyskinesia, a compulsive disorder or a panic disorder. The compounds associated with claims 102 to 110 are potent inhibitors of both acetylcholine esterase (AChE) and serotonin transport (SERT) (see the paragraph bridging pages 2 and 3 of the

present specification). As a consequence, they find utility in the treatment of conditions/diseases as laid out below.

(i) Depression

As pointed out in the paragraph bridging pages 1 and 2 of the present specification, SERT inhibitors are widely used in the treatment of depression. Compounds of the formula (I) are SERT inhibitors as stated in the paragraph bridging pages 2 and 3 of the specification, and as demonstrated in test example 1 and table 6 (pages 270 to 271 of the present specification). Consequently, it is respectfully submitted that claims to methods of treating depression using the compounds of claims 102 to 110 comply with all the requirements of 35 USC 112, first and second paragraphs.

(ii) Huntington's chorea

Huntington's chorea is characterized by cognitive impairment, dementia and psychosis, with rigidity and ataxia. The key neurotransmitter systems implicated in the disease are cholinergic and BABAergic systems in the chordate nucleus and putamen (see the enclosed copy of Manyam et al., J. Neurol., 237, (5), 281-284, 1990). Decreased CNS levels of

acetylcholine are linked to cognitive impairment and AChE inhibitors (such as those of the present claims) would be expected to alleviate this condition. The following studies further support this position.

Rivastigmine, an AChE inhibitor, has been demonstrated to reduce cognitive impairment and psychotic symptoms (see the enclosed copy of Rot et al., European Journal of Neurology: The Official Journal of the European Federation of Neurological Societies, 9, 689-690, 2002) and also to improve motor impairment (see the enclosed copy of de Thomaso et al., Movement Disorders, 19(12), 1516-1518, 2004). Recently, preclinical work indicates that SERT inhibitors would be useful in the treatment of Huntington's disease. This would further support the compliance of 35 USC 112 with respect to the use of the current compounds in the treatment of this disorder (see the enclosed copy of Duan et al., Neurol., 55, 590 to 594, 2004).

Furthermore, depression in Huntington's sufferers is common, with one recent study finding 70% of Huntington's sufferers reporting a history of treatment for depression (see the enclosed copy of Paulsen et al., Neuropsychiatry Clin. Neurosci., 7, 496 to 502, 2005). The compounds of the current

claims are SERT inhibitors, as well as AChE inhibitors, and as detailed above, are useful in the treatment of depression. As a consequence, it is respectfully submitted that claims to methods of treating Huntington's chorea using the present compounds satisfy all the requirements of 35 USC 112, first and second paragraphs.

(iii) Pick's disease

Pick's disease is associated with progressive loss of social skills, language and memory, and depression is also common. The condition is associated with abnormalities in the cholinergic and serotonergic systems (see the enclosed copy of Sparks et al., J. Neuropath. Exp. Neurol., 53(1), 37-42, 1994).

Cholinergic abnormalities suggest that the use of an acetylcholine esterase inhibitor might be effective in redressing the imbalance (see the enclosed copy of Perry and Miller, Neurology, 56 (Supplement 4), 546 to 551, 1990) (particularly see the text bridging pages 548 to 549)).

Furthermore, sufferers of Pick's disease display a variety of behavior symptoms, such as disinhibition, impulse control problems and aggression, known to be linked to a reduction of seratoninergic transmission (see the enclosed

copy of Swartz et al., J. Clin. Psychiatry, 58, pp. 212-216, 1997). These behavioral symptoms are treatable with SERT inhibitors, which are the drugs of choice for behavioral control in Pick's disease.

(iv) Tardive dyskinesia (TD)

Tardive dyskinesia (TD) is a movement disorder that is almost always caused by medications, particularly chronic use of typical antipsychotics. This gives rise to a hypersensitivity of dopamine receptors and subsequently to a doapamine/cholinergic imbalance in the basal ganglia.

The AChE inhibiting drugs, tacrine (see the enclosed copy of Ingram and Newgreen, Am. J. Psychiatry, 140, pp. 1629-1631, 1983) and donepezil (see the enclosed copy of Caroff et al., J. Clin. Psychiatry, 62, pp. 128-129, 2001) have been used in this condition and have been shown to reduce the symptoms of TD. Since the compounds of the present claims are also inhibitors of AChE, it is respectfully submitted that the use of these compounds in the treatment of TD would satisfy all the requirements of 35 USC 112, first and second paragraphs.

(v) Compulsive Disorders and Panic Disorders

In both of these conditions, the front line treatment option is currently SERT inhibitors. For example, see the enclosed copies of Fallon and Matthew, Journal of Psychiatric Practice, pp. 113-127, May 2000, and Sheehan, J. Clin. Psychiatry, 63 (Supp. 14), pp. 17-21, 2002). Consequently, it is respectfully submitted that claims to methods of treating compulsive disorders and panic disorders using the presently claimed compounds comply with all the requirements of 35 USC 112, first and second paragraphs.

Claims 111 to 117 and 131 to 133 are directed to a method of treatment of Alzheimer's disease using the presently claimed compounds.

Alzheimer's disease is characterized by a reduction in acetylcholine and reduced cholinergic function in the brain of sufferers. Clinical application of acetylcholine esterase inhibitors has been shown to be effective in treating the disease as pointed out on page 1 of the present specification in the paragraph entitled "Background Art."

Furthermore, in Alzheimer's sufferers, depression is a frequently reported symptom. SERT inhibitors are known in the

treatment of this condition (see the paragraph bridging pages 1 and 2 of the present specification and above). Consequently, it is respectfully submitted that claims to methods of treating Alzheimer's disease using the compounds of the present claims satisfy all the requirements of 35 USC 112, first and second paragraphs.

Very recently, a study demonstrating the effectiveness of donepezil (which is also an AchE inhibitor) has proven to be effective in improving mental function in patients with severe Alzheimer's disease (see the enclosed copy of Winblad et al., Lancet, e-pub., March 23, 2006).

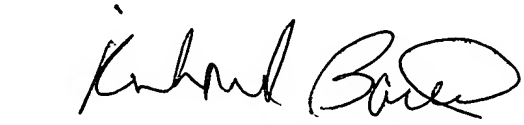
Withdrawal of the 35 USC 111, first and second paragraph rejections is thus respectfully requested.

Reconsideration is requested. Allowance is solicited.

An INFORMATION DISCLOSURE STATEMENT is being submitted concomitantly herewith.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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Enclosures: (1) PETITION FOR EXTENSION OF TIME
(2) INFORMATION DISCLOSURE STATEMENT, which includes copies of all the Manyan et al., Rof et al. de Thomas et al., Duran et al., Paulsen et al., Sparks et al., Perry et al., Swartz et al., Ingram et al., Caroff et al., Fallon et al. and Sheehan et al. publications cited above